

## PATENT COOPERATION TREATY

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 16 FEB 2005

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Applicant's or agent's file reference PPD70159WO		<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP 03/11725	International filing date (day/month/year) 23.10.2003	Priority date (day/month/year) 29.10.2002	
International Patent Classification (IPC) or both national classification and IPC C12N15/82			
Applicant SYNGENTA PARTICIPATIONS AG			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the opinion</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>			
Date of submission of the demand  06.04.2004		Date of completion of this report  14.02.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840		Authorized Officer  Schönwasser, D  Telephone No. +49 30 25901-318	



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP 03/11725

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-24 as originally filed

**Sequence listings part of the description, Pages**

1-30 as originally filed

**Claims, Numbers**

1-24 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application; the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.  
☒ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 22-24

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☒ the claims, or said claims Nos. 22-24 are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 22-24

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	4-21
	No: Claims	1-3
Inventive step (IS)	Yes: Claims	-
	No: Claims	1-21
Industrial applicability (IA)	Yes: Claims	1-21
	No: Claims	-

2. Citations and explanations

**see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

As outlined in the International Search Report (ISR), no search for subject-matter of claims 22-24 could be carried out due to insufficient support and disclosure according to Art. 5, and 6, PCT (see ISR, PCT/ISA form 210).

The applicant's attention is drawn to the fact that claims relating to subject-matter in respect of which no International Search Report has been established are usually not the subject of an International Preliminary Examination (Rule 66.1(e), PCT).

Hence, the present report does not relate to the subject-matter of the above mentioned claims.

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

- D1: WO 96/10083 A (CIBA GEIGY AG) 4 April 1996 (1996-04-04)
- D2: WO 02/078437 A (SYNGENTA PARTICIPATIONS AG) 10 October 2002 (2002-10-10)
- D3: WO 98/44137 A (NOVARTIS ERFIND VERWALT GMBH ;NOVARTIS AG (CH)) 8 October 1998 (1998-10-08)
- D4: DATABASE EM\_HTG [Online] 4 May 2002 (2002-05-04), BIRREN B. ET AL.: "Mus musculus clone RP24-217I1, WORKING DRAFT SEQUENCE, 4 unordered pieces" XP002273075 Database accession no. AC120146

**1. Novelty and Inventive step (Art. 33(2)(3), PCT)**

- 1.1** It is pointed out that the present International Preliminary Examination Report concerning novelty, inventive step and industrial applicability only refers to subject-matter for which an International Search Report has been established.

- 1.2 It is further noted that the document indicated in the search report as "PX" document has not been taken into consideration for the evaluation of novelty and inventive step, because the priority document of the present application has been **assumed** to be valid and the validity of priorities claimed by documents cited in the International Search Report will not be examined at the present stage (see also official Journal EPO, 11/2001, page 539-542, especially item 13).
- 1.3 The present application relates to plants, preferably cotton plants, which are transformed with a polynucleotide encoding the codon-optimised vegetative insecticidal protein VIP3A (originally isolated from *Bacillus sp.*) in order to render said transgenic plants resistant to insect attacks.  
Polynucleotides (SEQ ID NO:1,2 and 21), which comprise at least partly a fragment of the VIP3A expression cassette, transgenic plants and methods for detecting plant material derived from plant material transformed with a specific VIP3A expression cassette are claimed.
- 1.4 D1 discloses *inter alia* the protein sequence of VIP3A(a) (SEQ ID NO:29), which is 100% identical to the protein sequence of the VIP3a protein of the present application (SEQ ID NO:8) and the use of said protein for generating insecticidal plants by expressing said protein in plants, including cotton plants (p. 33, l. 21-22, p. 43, l. 4-18, Exp.18). Further, the detection of plant material expressing VIP3A protein by use of antibodies or nucleic acids or by measuring insect mortality is described (Exp. 18C, 18F and claim 108). The adaptation of the codon usage to the preferred host plant as well as the use of an actin promoter for driving VIP expression are also mentioned (p. 31, l.1-15; p. 101, l. 21-26).
- 1.5 D2 refers to VIP3 proteins and methods for generating transgenic plants expressing said insecticidal protein. In particular the expression of VIP3A (SEQ ID NO:5; 99.9 % identical to the VIP3A of the present application (SEQ ID NO:8)) in plants, *inter alia* in cotton plants, is described ([0004], [0017], Exp. 9). Further, the adaptation of the codon usage to the preferred host plant as well as the use of an actin promoter for driving VIP expression are also mentioned ([0081], [00115]).
- 1.6 D3 claims proteins of the VIP3 class, including VIP3A(a),VIP3A(b) and VIP3A(c), and transgenic plants, like e.g. cotton, expressing one of said toxic proteins (p. 2, l. 25-p.3, l.9; p. 6, l. 3-4). VIP3A(a) is 99.9% identical to the VIP3A protein of the present application (VIP3A(b) and VIP3A(c) show an identity of 99.5% and 98.8%, respectively). The detection of plant material expressing VIP3A protein by use of

antibodies or by measuring insect mortality is described (p. 29, l. 16-18; p. 30, l. 10-13) and it is suggested to use an actin promoter for expression of VIP3 in plants as well as to optimise codon usage of the VIP3 protein depending on the desired host plant.

- 1.7** D4 is a working draft sequence of a mouse clone, which overlaps in positions 116436-116456 with 21 contiguous nucleotides of SEQ ID NO:1. Consequently, subject-matter of claims 1-3 lacks novelty (Art. 33(2), PCT).
- 1.8** In view of D1-D3 all claims relating to VIP3A expressing plants including cotton plants (claims 10-12) and methods of detecting plant material expressing VIP3A (claims 13-21) are obvious and consequently lack inventive step (Art. 33(3), PCT).

Subject-matter of claims 1-8 refers to small polynucleotides (max. length 26 nt), which extend across the junctions where the VIP3A expression vector is inserted into the cotton genome. Taking into account that the expression vector consists of known elements (p. 14, l. 9-19) and the fact that the expression of VIP3A in cotton plants is known from the prior art (e.g. D1-D3), no inventive step can be acknowledged for such molecules, since it is generally known to the person skilled in the art how to design polynucleotides which extend across the junctions of a vector integration site.

In case inventive step could be established for the particular transgenic cotton plants of the application, **a use claim** directed to the polynucleotide sequences of claims 1-8 for detecting a vector integration event might be regarded as inventive in the sense of Art. 33(3), PCT.

The same objection concerning lack of inventive step also applies to subject-matter of claim 9, which comprises a coding sequence for VIP3A, which has been adapted to the codon preference of cotton plants, an expression vector of known elements and genomic cotton sequences 5' and 3' of the site of vector integration.

**2. Further remarks with regard to clarity (Art. 6, PCT)**

- 2.1** The term "COT102 event" is unclear. Hence claims 12, 13, 15, 18, 19, 21 and 22 are not in agreement with Art. 6, PCT.
- 2.2** Claim 10 refers to plants comprising a VIP3A protein and certain polynucleotides,

which comprise to a large extend sequences of the cotton genome (p. 13, l. 21-p. 13, l.3), i.e. they are **specific** for an insertion of the **VIP3A expression cassette into a cotton genome**. Hence, these polynucleotides should only be found in certain transgenic **cotton** plants, but not in other "non-cotton" plants.

- 2.3** The meaning of the term "COT102 bioassay profile" in claim 21 seems to be not clear from the description.